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calcium, metabolic conversion of arachidonate to thromboxane to prostacyclin and activation of intracellular protein kinases; wherein activation of platelets is additionally characterized by shape changes, secretory fusion of intracellular storage granules with plasma membranes and the vesiculation of membrane components from platelet surfaces; and wherein activation of endothelial cells is additionally characterized by secretion of high molecular weight multimers of the platelet adhesion protein, yon Willibrand Factor, and translocation of GMP140 to the endothelial cell surface,
and a pharmaceutically acceptable carrier.
5. The composition of claim 4 wherein the monoclonal antibody is a Fab fragment.

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L3: Entry 9 of 13 File: USPT Jun 3, 1997

DOCUMENT-IDENTIFIER: US 5635178 A
TITLE: Inhibition of complement mediated inflammatory response using monoclonal antibodies specific for a component forming the C56-9 complex which inhibit the platelet or endothelial cell activating function of the C56-9 complex

BSPR:
The classic complement pathway involves an initial antibody recognition of, and binding to, an antigenic site (SA) on a target cell. This surface bound antibody subsequently reacts with the first component of complement, C1q, forming a C1-antibody complex with Ca++, C1r, and C1s which is proteolytically active. C1s cleaves C2 and C4 into active components, C2a and C4a. The C4b,2a complex is an active protease called C3 convertase, and acts to cleave C3 into C3a and C3b. C3b forms a complex with C4b,2a to produce C4b,2a,3b, which cleaves C5 into C5a and C5b. C5b combines with C6. The C5b,6 complex combines with C7 to form the ternary complex C5b,6,7. The C5b,6,7 complex binds C8 at the surface of the cell, which may develop functional membrane lesions and undergo slow lysis. Upon binding of C9 to the C8 molecules in the C5b,6,7,8 complex, lysis of bacteria and other foreign cells is rapidly accelerated.

CLPR:
2. The method of claim 1 wherein an effective amount of said monoclonal antibody is administered to a patient in need of treatment for a disease selected from the group consisting of disseminated intravascular coagulation, lupus, rheumatoid arthritis, scleroderma, paroxysmal nocturnal hemoglobinuria, thrombotic thrombolytic purpura, vascular occlusion, reocclusion, coronary thrombosis, myocardial infarction, and complement mediated inflammatory vascular disorders.

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L3: Entry 9 of 13 File: USPT Jun 3, 1997

US-PAT-NO: 5635178
DOCUMENT-IDENTIFIER: US 5635178 A

TITLE: Inhibition of complement mediated inflammatory response using monoclonal antibodies specific for a component forming the C56-9 complex which inhibit the platelet or endothelial cell activating function of the C56-9 complex

DATE-ISSUED: June 3, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sims; Peter J.	Oklahoma City	OK		
Wiedmer; Therese	Oklahoma City	OK		

US-CL-CURRENT: 424/145.1; 530/388.25

CLAIMS:

We claim:
1. A method for inhibiting platelet or endothelial cell activation by complement proteins comprising:
administering to platelets and/or endothelial cells in an amount effective to inhibit platelet or endothelial cell activation a pharmaceutically acceptable composition comprising a monoclonal antibody which specifically binds to a component forming the C5b-9 complex and which inhibits the platelet or endothelial cell activating function of the C5b-9 complex wherein the platelet or endothelial cell activating function of the C5b-9 complex is characterized by initiation of a transient and reversible depolarization of the plasma membrane potential, a rise in cytosolic calcium, metabolic conversion of arachidonate to thromboxane to prostacyclin and activation of intracellular protein kinases; wherein activation of platelets is additionally characterized by shape changes, secretory fusion of intracellular storage granules with plasma membranes and the vesiculation of membrane components from platelet surfaces; and wherein activation of endothelial cells is additionally characterized by secretion of high molecular weight multimers of the platelet adhesion protein, yon Willibrand Factor, and translocation of GMP140 to the endothelial cell surface,
and a pharmaceutically acceptable carrier.
2. The method of claim 1 wherein an effective amount of said monoclonal antibody is administered to a patient in need of treatment for a disease selected from the group consisting of disseminated intravascular coagulation, lupus, rheumatoid arthritis, scleroderma, paroxysmal nocturnal hemoglobinuria, thrombotic thrombolytic purpura, vascular occlusion, reocclusion, coronary thrombosis, myocardial infarction, and complement mediated inflammatory vascular disorders.
3. The method of claim 1, wherein the monoclonal antibody is a Fab fragment.
4. A composition for intravenous injection into a patient comprising:
an effective amount to inhibit platelet or endothelial cell activation of a monoclonal antibody which specifically binds to a component forming the C5b-9 complex and which inhibits the platelet or endothelial cell activating function of the C5b-9 complex wherein the platelet or endothelial cell activating function of the C5b-9 complex is characterized by initiation of a transient and reversible depolarization of the plasma membrane potential, a rise in cytosolic

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L5: Entry 1 of 1 File: USPT Jun 3, 1997

US-PAT-NO: 5635178
DOCUMENT-IDENTIFIER: US 5635178 A

TITLE: Inhibition of complement mediated inflammatory response using monoclonal antibodies specific for a component forming the C56-9 complex which inhibit the platelet or endothelial cell activating function of the C56-9 complex

DATE-ISSUED: June 3, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sims; Peter J.	Oklahoma City	OK		
Wiedmer; Therese	Oklahoma City	OK		

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Oklahoma Medical Research Foundation	Oklahoma City	OK			02

APPL-NO: 8/ 207841
DATE FILED: March 8, 1994

PARENT-CASE:
This is a continuation of U.S. Ser. No. 07/813,432, filed Dec. 24, 1991 (abandoned), which is a divisional of U.S. Ser. No. 07/365,199 filed Jun. 12, 1989, issued on Aug. 4, 1992 as U.S. Pat. No. 5,135,916.

INT-CL: [6] A61K 39/395, C07K 16/18
US-CL-ISSUED: 424/145.1; 530/388.25
US-CL-CURRENT: 424/145.1; 530/388.25
FIELD-OF-SEARCH: 530/388.1, 530/388.25, 530/145.1, 424/141.1, 424/156.1, 424/130.1, 435/240.27

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

☐ Search Selected ☐ Search ALL

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	4447415	May 1984	Rock et al.	N/A
☐	4695460	September 1987	Holme	N/A
☐	4916219	April 1990	Linhardt et al.	N/A

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ART-UNIT: 186
PRIMARY-EXAMINER: Hutzell; Paula K.
ATTY-AGENT-FIRM: Arnall Golden & Gergory

ABSTRACT:

Compositions and methods for use thereof relating to monoclonal antibodies, and fragments thereof, having inhibitory activity towards the cell-activating function of the complement C5b-9 complex. The compositions can be used in vitro to inhibit C5b-9 related stimulatory responses of platelets and/or endothelial cells, thereby preventing C5b-9-initiated cell necrosis or stimulated secretion of proteolytic enzymes and the exposure of the procoagulant membrane receptors during collection and in vitro storage. Further, disease states can be treated by administering to platelets and/or endothelial cells in vivo an effective amount of a monoclonal antibody, or fragment thereof, which has inhibitory activity towards the cell-activating function of the C5b-9 complex, in a pharmaceutically acceptable carrier.

5 Claims, 9 Drawing figures

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ANTIBODEES.USPT,PGPB.	1
ANTIBODEIS.USPT,PGPB.	1
ANTIBODES.USPT,PGPB.	54
. . . . .	
BLOCK$(BLOCKS/TURN).USPT,PGPB.	pickup term
((COMPLEMENT OR C5) SAME (ANTIBOD$) SAME (ARTHRITIS OR JOINT) SAME (TREAT$ OR INHIBIT$ OR SUPPRESS$ OR PREVENT$ OR BLOCK$ OR THERAP$)).USPT,PGPB.	217

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USPT,PGPB	(c5) same (antibod$) and (arthritis or joint).clm.	13	L3
USPT,PGPB	(c5) same (antibod$) and (arthritis or joint)	176	L2
USPT,PGPB	(c5 or complement) same (antibod$) and (arthritis or joint)	1447	L1